REMARKS

The present invention features methods for reducing a neurological deficit in a patient who has suffered an injury to the central nervous system. In the methods now claimed, an epidermal growth factor-like (EGF-like) polypeptide is administered to the patient after a certain period of time has passed (*e.g.*, administration can begin six hours after the injury).

Claims 1-6, 17-18, and 25-43 are now pending in the application, claims 7-16 and 19-24 having been cancelled by the present amendment and claims 25-43 having been added. Claim 1 has been amended to specify that "administration of the EGF-like polypeptide commences more than 6 hours after the injury." This amendment is supported by original claim 14 (now cancelled). Two new independent claims have been added: claim 26, which specifies that "administration of the EGF-like polypeptide commences more than 12 hours after the injury" and claim 35, which specifies that "administration of the EGF-like polypeptide commences more than 24 hours after the injury." Claim 26 is supported by original claims 1 and 15 (now cancelled), and claim 35 is supported by claims 1 and 16 (now cancelled). Each of the independent claims is followed by a new dependent claim that specifies that the patient is a human patient (new dependent claims 25, 34, and 43). These claims are supported by the specification at, for example, page 17, lines 13-16). In addition, new independent claims 26 and 35 are followed by a set of dependent claims (claims 27-33 and 36-42) that, aside from their dependency, are identical to original claims 2-6, 17, and 18. No new matter has been added.

Drawings

The Examiner notes that "the instant specification contains sequences in Figure 1 and sequences presented in [a] separate [sequence] listing" (Office action at page 2). The Examiner suggests "that Fig. 1 is deleted in order not to duplicate the information" (Office action at page 2).

Applicants would prefer to retain Fig. 1 in their application. If the Examiner continues to believe it should be omitted, she is kindly asked to telephone the undersigned.

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Claims 1-6 and 14-18 were rejected as allegedly being obvious over Reynolds *et al.* (WO 98/221127; herein "Reynolds") in view of Peng *et al.* (*J. Cereb. Blood Flow & Metab.* 18:349-360, 1998; herein "Peng"). For the sake of completeness and easy reference, the Examiner's argument is reproduced here.

With respect to Reynolds, the Examiner states (Office action at page 3):

> Reynolds et al. discloses methods for protecting neural tissue from the effects of insult, and neurological diseases or disorders by administering growth factors (EGF in particular) to the neural tissue of a mammal (see the abstract, also page 4, line 2, Example 2 on page 12 and claims 11-15). Neurodegenerative diseases, which intended to be treated by methods of Reynolds et al. include stroke and physical trauma to the central nervous system (page 1, lines 9 and 14). The document of Reynolds et al. teaches exogenous administration of EGF for such treatment (page 4, lines 9-13 and pages 8-9). Reynolds et al. do not expressly disclose a method of administration of EGF for reducing a neurological deficit in a patient with an injury to the CNS wherein administration of EGF commences more than 6, 12, or 24 hours after the injury.

With respect to Peng, the Examiner states (Office action at pages 3-4):

> Peng et al. [d]isclose the information about EGF being a protective factor against forebrain ischemia-induced injuries (see the abstract). Peng et al. taught post-ischemic infusion of EGF (page 350, second column, last paragraph and page 351, first column, first paragraph) to reduce neuronal damage caused by forebrain ischemia. According to Peng et al. experiments were done where EGF was infused into cerebral ventricles of ischemic animals after 3-minute forebrain ischemia and continued for seven days.

The Examiner then concludes (Office action at page 4):

> At the time the instant invention was made, it would have been obvious to a person of ordinary skill in the art to use the information provided by Peng et al. in the methods disclosed by Reynolds et al. One of ordinary skill in the art would have been motivated to do this because the disclosure of Reynolds et al. teaches methods for treating and protecting neural tissue from ischema and trauma by administration of EGF before the insult or as a preventative measure and disclosure of Peng et al. teaches the beneficial effects of EGF on ischemia-induced neuronal damage even during post-ischemic administration.

There is no *prima facie* case of obviousness, because the prior art does not teach all the limitations of the method now claimed.

In view of the present amendment, the rejection for obviousness should be withdrawn (this is not an admission that original claims 1-6 and 14-18 were obvious in view of the prior art; Applicant does not believe they were and expressly retains the right to prosecute those claims in a later filed application).

As set out in the MPEP, three basic criteria must be met in order to establish *prima facie* obviousness: (1) there must be some suggestion or motivation to modify a prior art reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the limitations of the claim. MPEP at 2142.

In the present case, neither Reynolds nor Peng suggest administration of EGF more than six, 12, or 24 hours after an injury to the CNS. In fact, with respect to Reynolds, the Examiner has already found as much. The Examiner has stated, "Reynolds et al. do not expressly disclose a method of administration of EGF for reducing a neurological deficit in a patient with an injury to the CNS wherein administration of EGF commences more than 6, 12, or 24 hours after the injury." Indeed, Reynolds is strictly limited to *neuroprotection*, and advocates only methods in which a growth factor is administered *prior to* the onset of trauma or the manifestations of neurological disease or aging (*see, e.g.*, the Abstract and page 4, lines 14-17). Thus, if there is any suggestion that one should administer an EGF-like polypeptide more than six, 12, or 24 hours after an injury, it must be found in Peng, and we turn to that reference now.

With respect to Peng's experiments, the Examiner states, "EGF was infused into cerebral ventricles of ischemic animals after 3-minute forebrain ischemia and continued for seven days." The infusion commenced, however, either prior to the ischemia or immediately afterward. Peng states (Abstract; emphasis added; *see also* the descriptions of infusions bridging pages 350-351):

> Cerebroventricular infusion of EGF (24 or 120 ng/d) for 7 days to gerbils *starting 2 hours before or immediately after transient forebrain sichemia* caused a significant prolongation of response latency time in a passive avoidance task in comparison with the response latency of vehicle-treated ischemic animals.

Nothing in Peng suggests that one should administer an EGF-like polypeptide more than six, 12, or 24 hours after an injury. Thus, neither of the prior art references suggests all the limitations of the present claims. On this basis alone, the rejection for obviousness must be withdrawn.

CONCLUDING REMARKS

Applicant asks that all claims be allowed. Attached is a marked-up version of the claim being amended by the current amendment. Enclosed is a check in the amount of $27 for excess claim fees, a Petition for a one-month extension of time, and a check for the extension fee ($55). Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 14-16 have been cancelled.

Claims 1 has been amended as follows.

1. (Amended) A method for reducing a neurological deficit in a patient who has suffered an injury to the central nervous system, the method comprising administering to the patient an amount of an epidermal growth factor-like (EGF-like) polypeptide effective to reduce [a] the neurological deficit in the patient, wherein administration of the EGF-like polypeptide commences more than 6 hours after the injury.